

## WHAT IS CLAIMED IS:

1. A method for sterilizing a preparation of urokinase that is sensitive to radiation, said method comprising irradiating said preparation of urokinase with radiation for a time effective to sterilize said preparation of urokinase at a rate effective to sterilize said preparation of urokinase and to protect said preparation of urokinase from said radiation.

2. A method for sterilizing a preparation of urokinase that is sensitive to radiation, said method comprising:

(i) applying to said preparation of urokinase at least one stabilizing process selected from the group consisting of:

- (a) adding to said preparation of urokinase at least one stabilizer;
- (b) reducing the residual solvent content of said preparation of urokinase;
- (c) reducing the temperature of said preparation of urokinase;
- (d) reducing the oxygen content of said preparation of urokinase;
- (e) adjusting or maintaining the pH of said preparation of urokinase; and
- (f) adding to said preparation of urokinase at least one non-aqueous solvent; and

(ii) irradiating said preparation of urokinase with a suitable radiation at an effective rate for a time effective to sterilize said preparation of urokinase, wherein said at least one stabilizing process protects said preparation of urokinase from said radiation.

3. A method for sterilizing a preparation of urokinase that is sensitive to radiation, said method comprising irradiating said preparation of urokinase with radiation to a total dose effective to sterilize said preparation of urokinase at a rate effective to sterilize said preparation of urokinase and to protect said preparation of urokinase from said radiation.

4. The method according to claim 2, wherein said residual solvent is an organic solvent.

5. The method according to claim 2, wherein said residual solvent is an aqueous solvent.

6. The method according to claim 2, wherein said stabilizing process and said rate are together effective to protect said preparation of urokinase from said radiation.

7. The method according to claim 2, wherein at least two stabilizing processes are applied and said at least two stabilizing processes are together effective to protect said preparation of urokinase from said radiation.

8. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of not more than 3.0 kGy/hour.

9. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of not more than 2.5 kGy/hr.

10. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of not more than 2.0 kGy/hr.

11. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of not more than 1.0 kGy/hr.

12. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of not more than 0.3 kGy/hr.

13. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of more than 3.0 kGy/hour.

14. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of at least 5.0 kGy/hour.

15. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of at least 18.0 kGy/hour.

16. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of at least 30.0 kGy/hour.

17. The method according to claim 1, 2 or 3, wherein said effective rate comprises a rate of at least 45 kGy/hour.

18. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is maintained in a low oxygen atmosphere.

19. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is maintained in an atmosphere comprising at least one noble gas or nitrogen.

20. The method according to claim 19, wherein said noble gas is argon.

21. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is maintained in a vacuum.

22. The method according to claim 2, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of solute, evaporation, chemical extraction, spray-drying and vitrification.

23. The method according to claim 2, wherein said residual solvent content is less than about 15%.

24. The method according to claim 2, wherein said residual solvent content is less than about 10%.

25. The method according to claim 2, wherein said residual solvent content is less than about 3%.

26. The method according to claim 2, wherein said residual solvent content is less than about 2%.

27. The method according to claim 2, wherein said residual solvent content is less than about 1%.

28. The method according to claim 2, wherein said residual solvent content is less than about 0.5%.

29. The method according to claim 2, wherein said residual solvent content is less than about 0.08%.

30. The method according to claim 1, 2 or 3, wherein at least one sensitizer is added to said preparation of urokinase prior to said step of irradiating said preparation of urokinase.

31. The method according to claim 2, wherein said at least one stabilizer is an antioxidant.

32. The method according to claim 2, wherein said at least one stabilizer is a free radical scavenger.

33. The method according to claim 2, wherein said at least one stabilizer is a ligand.

34. The method according to claim 33, wherein said ligand is heparin.

35. The method according to claim 2, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

36. The method according to claim 2, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; vitamin E or a derivative thereof; albumin; sucrose; glycylglycine; L-carnosine; cysteine; silymarin; diosmin; hydroquinonesulfonic acid; 6-hydroxy-2,5,7,8-tetramethylchroman-2-

carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine; lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; propyl gallate; ethanol; acetone; rutin; epicatechin; biacalein; purpurogallin; pyruvate; lactate; and mixtures of two or more thereof.

37. The method according to claim 36, wherein said mixtures of two or more stabilizers are selected from the group consisting of: mixtures of ethanol and acetone; mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and albumin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, albumin and sucrose; mixtures of ascorbic acid, or a salt or ester thereof, and glycylglycine; mixtures of ascorbic acid, or a salt or ester thereof, glycylglycine and albumin; mixtures of ascorbic acid, or a salt or ester thereof, and L-carnosine; mixtures of ascorbic acid, or a salt or ester thereof, and cysteine; mixtures of ascorbic acid, or a salt or ester thereof, and N-acetyl cysteine; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, and silymarin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, 6-hydroxy-2,5,7,8-tetramethylchroman-2-

carboxylic acid, and diosmin; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and lipoic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and hydroquinonesulfonic acid; mixtures of pyruvate and lactate; mixtures of pyruvate and ascorbate, or a salt or ester thereof; mixtures of pyruvate and histidine; and mixtures of uric acid, or a salt or ester thereof, lipoic acid, sodium formaldehyde sulfoxylate, gallic acid, or a derivative thereof, propyl gallate, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid.

38. The method according to claim 2, wherein said at least one stabilizer is a dipeptide stabilizer.

39. The method according to claim 38, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine and anserine.

40. The method according to claim 2, wherein said at least one stabilizer inhibits the generation of free radicals.

41. The method according to claim 2, wherein said at least one stabilizer inhibits the generation of reactive oxygen species.

42. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 200 mM.



43. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 1 mM.

44. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 2 mM.

45. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 5 mM.

46. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 10 mM.

47. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 25 mM.

48. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 50 mM.

49. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of at least 100 mM.

50. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of from 0.1 mM to 10 mM.

51. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of from 0.1 mM to 50 mM.

52. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of from 10 mM to 100 mM.

53. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of from 10 mM to 50 mM.

54. The method according to claim 2, wherein said at least one stabilizer is present in a concentration of from 50 mM to 100 mM.

55. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is about ambient temperature at the initiation of said irradiation.

56. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below ambient temperature at the initiation of said irradiation.

57. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below the freezing point of said preparation of urokinase at the initiation of said irradiation.

58. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below the eutectic point of said preparation of urokinase at the initiation of said irradiation.

59. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is above ambient temperature at the initiation of said irradiation.

60. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -75°C at the initiation of said irradiation.

61. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -70°C at the initiation of said irradiation.

62. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -55°C at the initiation of said irradiation.

63. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -50°C at the initiation of said irradiation.

64. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -40°C at the initiation of said irradiation.

65. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -30°C at the initiation of said irradiation.

66. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -20°C at the initiation of said irradiation.

67. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -10°C at the initiation of said irradiation.

68. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least 4°C at the initiation of said irradiation.

69. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is about the same temperature as dry ice at the initiation of said irradiation.

70. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -55°C at the initiation of said irradiation.

71. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -50°C at the initiation of said irradiation.

72. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -30°C at the initiation of said irradiation.

73. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -30°C and -70°C at the initiation of said irradiation.

74. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -30°C and -50°C at the initiation of said irradiation.

75. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -40°C and -55°C at the initiation of said irradiation.

76. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -40°C and -50°C at the initiation of said irradiation.

77. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 100% of the pre-irradiation value.

78. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is greater than 100% of the pre-irradiation value.

79. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is at least 95% of the pre-irradiation value.

80. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 90% of the pre-irradiation value.

81. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 85% of the pre-irradiation value.

82. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 80% of the pre-irradiation value.

83. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 70% of the pre-irradiation value.

84. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 60% of the pre-irradiation value.

85. The method according to claim 1, 2 or 3, wherein the functional activity of said preparation of urokinase after sterilization by irradiation is about 50% of the pre-irradiation value.

86. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 105 kGy.

87. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 90 kGy.

88. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 80 kGy.

89. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 70 kGy.

90. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 65 kGy.

91. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 55 kGy.

92. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 50 kGy.

93. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 40 kGy.

94. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 30 kGy.

95. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 25 kGy.



96. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is irradiated to a total dose of at least 10 kGy.

97. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 7.

98. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 6.

99. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 5.

100. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 4.

101. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 3.

102. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 2.

103. The method according to claim 1, 2 or 3, wherein said preparation of urokinase has a pH of less than 1.

104. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is a mammalian preparation of urokinase.

105. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is a bovine preparation of urokinase.

106. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is an ovine preparation of urokinase.

107. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is a porcine preparation of urokinase.

108. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is an equine preparation of urokinase.

109. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is a caprine preparation of urokinase.

110. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is obtained from a fetal, immature or adult mammal.

112. The method according to claim 1, 2 or 3, wherein said preparation of urokinase contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, parasites and prions or similar agents responsible, alone or in combination, for TSEs.

113. The method according to claim 1, 2 or 3, wherein said effective rate is constant throughout said irradiation.

114. The method according to claim 1, 2 or 3, wherein said effective rate is not constant throughout said irradiation.

115. The method according to claim 114, wherein said effective rate is less than 3.0 kGy/hr for at least a portion of said irradiation.

116. The method according to claim 1, 2 or 3, wherein said irradiating is performed under conditions whereby the temperature of said preparation of urokinase increases during said irradiating from an initial temperature ( $T_i$ ) to a final temperature ( $T_f$ ) and further

wherein said increase in the temperature of said preparation of urokinase ( $\Delta T$ ) is about equal to the total dose of said radiation (D) divided by the specific heat constant of said preparation of urokinase (c).

117. The method according to claim 116, wherein said final temperature ( $T_f$ ) is at or below a temperature effective to protect said preparation of urokinase from said radiation.

118. The method according to claim 116, wherein said increase in the temperature of said preparation of urokinase ( $\Delta T$ ) is about  $0.25^\circ\text{C}/\text{kGy}$ .

119. The method according to claim 2, wherein said residual solvent content is reduced by the addition of an effective amount of at least one solute.

120. The method according to claim 2, wherein said residual solvent content is reduced by lyophilization.

121. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is about ambient temperature for at least a portion of said irradiation.

122. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below ambient temperature for at least a portion of said irradiation.

123. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below the freezing point of said preparation of urokinase for at least a portion of said irradiation.

124. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below the eutectic point of said preparation of urokinase for at least a portion of said irradiation.

125. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is above ambient temperature for at least a portion of said irradiation.

126. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -75°C for at least a portion of said irradiation.

127. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -70°C for at least a portion of said irradiation.

128. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -55°C for at least a portion of said irradiation.

129. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -50°C for at least a portion of said irradiation.

130. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -40°C for at least a portion of said irradiation.

131. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -30°C for at least a portion of said irradiation.

132. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -20°C for at least a portion of said irradiation.

133. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least -10°C for at least a portion of said irradiation.

134. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is at least 4°C for at least a portion of said irradiation.

135. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is about the same temperature as dry ice for at least a portion of said irradiation.

136. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -55°C for at least a portion of said irradiation.

137. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -50°C for at least a portion of said irradiation.

138. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -10°C and -30°C for at least a portion of said irradiation.

139. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -30°C and -70°C for at least a portion of said irradiation.

140. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -30°C and -50°C for at least a portion of said irradiation.

141. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -40°C and -55°C for at least a portion of said irradiation.

142. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is between -40°C and -50°C for at least a portion of said irradiation.

143. The method according to claim 2, wherein said residual solvent content of said preparation of urokinase is reduced to a level between 0.5% and 5.0% prior to said irradiation.

144. The method according to claim 2, wherein said residual solvent content of said preparation of urokinase is reduced to a level between 0.5% and 2.5% prior to said irradiation.

145. The method according to claim 2, wherein said residual solvent content of said preparation of urokinase is reduced to a level between 1.0% and 10.0% prior to said irradiation.

146. The method according to claim 2, wherein said residual solvent content of said preparation of urokinase is reduced to a level between 2.5% and 10.0% prior to said irradiation.

147. The method according to claim 2, wherein said at least one stabilizer comprises at least one  $\alpha$ -keto acid.



148. The method according to claim 1, 2 or 3, wherein the temperature of said preparation of urokinase is below the glass transition temperature of said preparation of urokinase at the initiation of said irradiation.

149. The method according to claim 1, 2 or 3, wherein said preparation of urokinase is obtained from a mammal.

150. The method according to claim 8, wherein said effective rate further comprises a rate of more than 3.0 kGy/hour.

151. The method according to claim 9, wherein said effective rate further comprises a rate of more than 2.5 kGy/hr.

152. The method according to claim 10, wherein said effective rate further comprises a rate of more than 2.0 kGy/hr.

153. The method according to claim 11, wherein said effective rate further comprises a rate of more than 1.0 kGy/hr.

154. The method according to claim 12, wherein said effective rate further comprises a rate of more than 0.3 kGy/hr.

155. The method according to claim 8, wherein said effective rate further comprises a rate of at least 5.0 kGy/hour.

156. The method according to claim 8, wherein said effective rate further comprises a rate of at least 18.0 kGy/hour.

157. The method according to claim 8, wherein said effective rate further comprises a rate of at least 30.0 kGy/hour.

158. The method according to claim 8, wherein said effective rate further comprises a rate of at least 45 kGy/hour.

159. The method according to claim 9, wherein said effective rate further comprises a rate of at least 5.0 kGy/hour.

160. The method according to claim 9, wherein said effective rate further comprises a rate of at least 18.0 kGy/hour.

161. The method according to claim 9, wherein said effective rate further comprises a rate of at least 30.0 kGy/hour.

162. The method according to claim 9, wherein said effective rate further comprises a rate of at least 45 kGy/hour.

163. The method according to claim 10, wherein said effective rate further comprises a rate of at least 5.0 kGy/hour.

164. The method according to claim 10, wherein said effective rate further comprises a rate of at least 18.0 kGy/hour.

165. The method according to claim 10, wherein said effective rate further comprises a rate of at least 30.0 kGy/hour.

166. The method according to claim 10, wherein said effective rate further comprises a rate of at least 45 kGy/hour.

167. The method according to claim 11, wherein said effective rate further comprises a rate of at least 5.0 kGy/hour.

168. The method according to claim 11, wherein said effective rate further comprises a rate of at least 18.0 kGy/hour.

169. The method according to claim 11, wherein said effective rate further comprises a rate of at least 30.0 kGy/hour.

170. The method according to claim 11, wherein said effective rate further comprises a rate of at least 45 kGy/hour.

171. The method according to claim 12, wherein said effective rate further comprises a rate of at least 5.0 kGy/hour.

172. The method according to claim 12, wherein said effective rate further comprises a rate of at least 18.0 kGy/hour.

173. The method according to claim 12, wherein said effective rate further comprises a rate of at least 30.0 kGy/hour.

174. The method according to claim 12, wherein said effective rate further comprises a rate of at least 45 kGy/hour.

175. The method according to claim 1, 2 or 3, wherein said effective rate is not constant.

176. The method according to claim 1 or 2, wherein said effective rate is not constant for at least a portion of said time effective to sterilize said preparation of urokinase.